REMARKS

Claims 1-14 are pending in this application. Claims 1-10 and 12-14 are rejected. Claim 11 is allowed. New claims 22-28, which depend directly or indirectly on claim 11, are added. Claim 12 is amended to correct a typographical error. The amendment of claim 12 is not intended to narrow the scope of the claim. No new matter is added by this Amendment. Applicant respectfully submits that the pending claims are allowable for at least the following reasons.

The Rejection of Claims 1-10 And 12-14 Under 35 U.S.C. § 103(a) Over Pham In View of Olah Should Be Withdrawn

Claims 1-10 and 12-14 were rejected under 35 U.S.C. § 103(a) over U.S. Patent No. 5,663,474 to Pham *et al.* ("Pham") in view of U.S. Patent No. 5,073,674 to Olah ("Olah"). Claims 2-10 and 12-14 depend on claim 1 directly or indirectly. The Examiner indicated that (1) Pham discloses an alkylation process of aliphatic or aromatic hydrocarbons with an olefin in the presence of a solid polymeric hydrogen fluoride catalyst; and (2) Olah discloses that liquid onium polyhydrogen fluoride can be used as a safe alkylation catalyst. (Office Action at p. 3.) The Examiner then asserted that:

> "It would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the Pham process by using liquid onium polyhydrogen fluoride in the place of hydrogen fluoride of the Pham catalyst since it is expected that using polyhydrogen fluoride or hydrogen fluoride would yield similar results. Applicants are reminded that it has been established that closely related homologs, analogs and isomers in chemistry may create a prima facie case of obviousness."

(Office Action at p. 4.) Applicant respectfully submits that the Examiner has failed to establish a *prima facie* case of obviousness because polyhydrogen fluoride and hydrogen fluoride are neither closely related nor homologs, analogs and isomers. Even assuming arguendo that the Examiner had established a *prima facie* case of obviousness, the presumption of obviousness is overcome as demonstrated below.

A) The Examiner Failed To Establish A *Prima Facie* Case Of Obviousness

To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine reference teachings. *In re Rouffet*, 149 F.3d 1350, 1357, 47 USPQ2d 1453,1457-58 (Fed. Cir. 1998). Second, there must be a reasonable expectation of success. *In re Merck & Co.,*

Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. *In re Royka*, 490 F.2d 981, 180 USPQ 580 (CCPA 1974). Applicant respectfully submits that the Examiner failed to establish a *prima facie* case of obviousness because (1) the prior art references, individually or in combination, do not teach or suggest all the claim limitations; (2) there is a lack of motivation to combine the teachings in the cited references; and (3) the references actually teach away from the invention.

Pham teaches a solid polymeric hydrogen fluoride catalyst comprising a polymer carrier and hydrogen fluoride (HF) wherein the polymer carrier is not a reactant in the alkylation reaction and "does not form a complex with hydrogen fluoride." (Pham, col. 1, lines 41-56; and col. 2, lines 17-22.) Olah discloses a liquid onium polyhydrogen fluoride complex of hydrogen fluoride and a non-polymeric molecule such as ammonia and an amine. (Olah, col. 1, lines 58-68.) Claim 1 as presently pending recites the element of "a solid polymeric onium polyhydrogen fluoride complex" which refers to any solid polymeric or oligomeric material containing in some or all of its repeating units an atom capable of forming an onium fluoride moiety with hydrogen fluoride (HF). (*See* the specification of this application at p. 3, lines 16-23.)

The cited references, Olah and Pham, individually or in combination, do not teach or suggest all the claim limitations of claim 1, particularly the limitation of a solid complex, *i.e.*, the solid polymeric onium polyhydrogen fluoride complex, as discussed below. The Examiner asserted that it is obvious to modify the Pham process "by using liquid onium polyhydrogen fluoride (complex) in the place of hydrogen fluoride of the Pham catalyst since it is expected that using polyhydrogen fluoride (complex) or hydrogen fluoride would yield similar results." Applicant respectfully submits that a modification of the Pham process by replacing the HF in the solid catalyst of Pham with the liquid onium polyhydrogen fluoride complex of Olah will not, according to Pham's teachings, result in a solid complex but a physical mixture of (1) a polymer and (2) the liquid complex of Olah. Indeed, Pham teaches that the polymer in Pham's catalyst cannot form a complex with HF. Therefore, no solid polymeric onium polyhydrogen fluoride complex is expected to form.

Furthermore, the cited references, Olah and Pham, not only do not teach or suggest all the claim limitations of claim 1, but also teach away from the claimed invention. *In re Fine*, 837 F.2d 1071 (Fed. Cir. 1988). Pham teaches away from using a solid complex in its disclosure at col. 1, lines 53-56, *i.e*, the polymer carrier "does not form a complex with hydrogen fluoride." The absence of a solid complex or the expectation to form one results in a teaching

away from the instant invention. Further, Olah merely teaches a liquid complex. Based on the comments above, the obviousness rejections of claim 1 and all claims depending on claim 1, *i.e.*, claims 2-10 and 12-14, under 35 U.S.C. § 103(a) over Pham in view of Olah are improper and should be withdrawn.

(B) Polyhydrogen Fluoride And Hydrogen Fluoride Are Neither Closely Related Nor Homologs, Analogs And Isomers.

The Examiner argued that a *prima facie* case of obviousness was established because polyhydrogen fluoride and hydrogen fluoride are "closely related homologs, analogs and isomers in chemistry." (Office Action at p. 4.) The Examiner cited cases to support the alleged *prima facie* case of obviousness. *In re Dillion*, 16 USPQ 2d 1897 (Fed. Cir. 1990); *In re Payne*, 203 USPQ 245 (CCPA 1979); *In re Mills*,126 USPQ 513 (CCPA 1960); *In re Henze*, 85 USPQ 261 (CCPA 1950); *In re Haas*, 60 USPQ 544 (CCPA 1944). The cases relied upon by the Examiner merely establish that if an Examiner considers that he has found prior art close enough to the claimed invention to give one skilled in the relevant chemical art the motivation to make close relatives (homologs, analogs, isomers, etc.) of the prior art compound(s), then there arises a *prima facie* case of obviousness. *In re Henze*, 85 USPQ 261 (CCPA 1950); *In re Haas*, 60 USPQ 544 at 548, 552 (CCPA 1944). The teaching or suggestion to modify the structure must be found in the references cited by the Examiner. *In re Kotzab*, 217 F.3d 1365, 1370, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000). Conclusory statements of the Examiner are not enough. *In re Lee*, 61 USPQ2d 1430 (Fed. Cir. 2002).

Applicant respectfully submits that polyhydrogen fluoride and hydrogen fluoride are neither closely related nor homologs, analogs and isomers in chemistry, and therefore the Examiner has failed to establish a *prima facie* case of obviousness.

The definitions of homolog, analog and isomer under the IUPAC (International Union Of Pure And Applied Chemistry) nomenclature system are as follows. A homologue means "a compound belonging to a series of compounds differing from each other by a repeating unit, such as a methylene group, a peptide residue, etc." Wermuth *et al.*, "Glossary of terms used in Medicinal Chemistry (IUPAC Recommendations 1998)," *Pure & Appl. Chem.*, 1998, **70**, 1129-1143 at 1137. (Attached as reference #1.) Under IUPAC, an analog means "a drug whose structure is related to that of another drug but whose chemical and biological properties may be quite different." (*id.* at 1131.) Furthermore, a chemical analog refers to "a structure derivative of a parent compound that often differs from it by a single element." *American Heritage College*

Dictionary, Third Edition, Houghton Mifflin Company, Boston, p. 48 (1997). (Attached as reference #2.) An isomer means "one of several chemical species (or molecular entities) that have the same stoichiometric molecular formula but different constitutional formulae or different stereochemical formulae and hence potentially different physical and/or chemical properties." G.P. Moss, "Basic Terminology of Stereochemistry (IUPAC Recommendations 1996)," *Pure & Appl. Chem.*, 1996, **68**, 2193-2222 at 2210. (Attached as reference #3.)

Hydrogen fluoride is a neutral molecule having the formula of HF whereas polyhydrogen fluoride is an anion having the formula of $F(HF)^-_m$. (*See* the specification of this application at p. 4, line 15.) In general, polyhydrogen fluoride does not exist alone but co-exists with its counter-cation in the liquid or solid onium polyhydrogen fluoride complex.

Under the IUPAC definition, polyhydrogen fluoride is not an analog of HF because their structures are not closely related since the former is an anion of a complex and the latter is a neutral molecule. Under the dictionary meaning, they are not chemical analog because they differ from each other by more than a single element.

Further, polyhydrogen fluoride is not a homolog of HF because they do not belong to a series of compounds differing from each other by a repeating unit because they do not belong to the same series of compounds. As a matter of fact, polyhydrogen fluoride is an anion but not a compound.

Further, polyhydrogen fluoride is not an isomer of HF because they do not have the same stoichiometric molecular formula.

Further, polyhydrogen fluoride is not closely related to HF because (1) they have very different chemical formulae; and (2) they belong to different classes of chemical, i.e., the former is an anion of a complex and the latter is a neutral molecule.

The chemical difference between the liquid onium polyhydrogen fluoride complex and HF is even greater than that between polyhydrogen fluoride and HF because the liquid onium polyhydrogen fluoride complex, in addition to the polyhydrogen fluoride anion, further contains a cation and HF does not.

Therefore, HF is not closely related to polyhydrogen fluoride or the liquid onium polyhydrogen fluoride complex.

Based on the comments above, the obviousness rejections of claim 1 and all claims depending on claim 1, *i.e.*, claims 2-10 and 12-14, under 35 U.S.C. § 103(a) over Pham in view of Olah are improper and should be withdrawn.

(C) Even If The Examiner Had Established A *Prima Facie* Case Of Obviousness, The Presumption Of Obviousness Could Be Overcome.

The Examiner asserted that a *prima facie* case was established because of the close similarity between polyhydrogen fluoride and HF. As mentioned earlier, polyhydrogen fluoride and HF are not closely related and the Examiner has failed to established a *prima facie* case of obviousness. Even if the Examiner had established a *prima facie* case of obviousness, the alleged presumption of obviousness could be overcome for the following reasons.

A presumption of obviousness based on close structural similarity is overcome where the prior art does not disclose or render a method for making the claimed compound. *In re Payne*, 203 USPQ 245 at 255 (CCPA 1979). The cited references, Olah and Pham, individually or in combination, do not teach or disclose a method for making the solid polymeric onium polyhydrogen fluoride complex of claim 1. Olah merely discloses a method of making a liquid onium polyhydrogen fluoride complex of a non-polymeric molecule and HF. Pham only discloses a method of making a solid catalyst comprise a polymer carrier and HF. More importantly, Pham teaches away from the invention because it discloses that the polymer and HF do not form a complex. Therefore, the combined references do not teach or motivate a person skilled in the art to make a solid complex of claim 1.

Furthermore, the mere fact that it is possible to find two isolated disclosures which might be combined in such a way to produce a new compound does not necessarily render such production obvious unless the art also contained something to suggest the desirability of the proposed combination. *In re Grabiak*, 769 F.2d 729 at 732 citing *In re Bergel*, 292 F.2D 955 at 956-957. The Applicant respectfully submits that there is no pertinent reference showing or suggesting the desirability of the modification of the Pham process by using liquid onium polyhydrogen fluoride complex in the place of hydrogen fluoride. To the contrary, Pham teaches that the polymer of Pham "does not form a complex with hydrogen fluoride." (Pham, col. 1, lines 53-56.) If there is no complex formation, there will not have a solid complex. Therefore, the cited references would not have motivated a person of ordinary skill in the art to combine the teachings in the cited references to provide the solid complex in claim 1.

Based on the comments above, the obviousness rejections of claim 1 and all claims depending on claim 1, *i.e.*, claims 2-10 and 12-14, under 35 U.S.C. § 103(a) over Pham in view of Olah are overcome.

In view of all the comments in (A)-(C), Applicants respectfully request withdrawal of the rejection of claim 1 and other claims, *i.e.*, 2-10 and 12-14, depending on claim 1 under 35 U.S.C. § 103(a) over Pham in view of Olah.

ALLOWABLE SUBJECT MATTER

The Examiner indicated that the subject matter claimed in claim 11 is allowable. New claims 22-28 depend on claim 11 and therefore they are also allowable.

CONCLUSION

In view of the foregoing, it is submitted that this application is in condition for allowance. Favorable consideration and prompt allowance of the application are respectfully requested.

The Examiner is invited to telephone the undersigned if the Examiner believes it would be useful to advance prosecution.

No fee is believed due for this Amendment. However, if a fee is due, please charge such fee to Jones Day Deposit Account No. 50-3013 (order no. 702904-999018)

Respectfully submitted,

Date: July 26, 2005

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INTERNATIONAL UNION OF PURE AND APPLIED CHEMISTRY

CHEMISTRY AND HUMAN HEALTH DIVISION
MEDICINAL CHEMISTRY SECTION

GLOSSARY OF TERMS USED IN MEDICINAL CHEMISTRY

(IUPAC Recommendations 1998)

Prepared for publication by

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Glossary of terms used in medicinal chemistry (IUPAC Recommendations 1998)

Abstract: The objective of the glossary is to provide in a single document a consistent terminology and concise definitions of terms covering the various aspects of medicinal chemistry. This was felt necessary with regard to the rapid changes occuring in medicinal chemistry and also by the need to establish international definition standards. Effectively the possibility exists that in different countries certain terms may not have the same meaning, in such a case the creation of an internationally accepted definition is particularly justified.

A Working Party belonging to the IUPAC Section on Medicinal Chemistry has therefore been assembled which prepared the present glossary. Concise but sufficiently explanatory definitions have been formulated for about one hundred commonly employed terms which can be considered of particular interest to the medicinal chemistry community. The glossary has been compiled in part from definitions proposed by the Working Party in part from earlier IUPAC glossaries and in part from well-accepted definitions taken from the literature but which were sometimes published in journals or books that may not be readily accessible.

ALPHABETICAL ORDERED ENTRIES

The glossary has been compiled in part from definitions proposed by the Working Party and in part from well-accepted definitions taken from the literature. In most cases, definitions given here are for specific areas of medicinal chemistry. Some definitions taken from the Glossary for Chemists of Terms Used in Biotechnology (*Pure Appl. Chem.*, 1992, **64**, 143–168) were also included, eventually in a slightly modified form; they are identified by an asterisk*. Others, which appear in the Glossary on Computational Drug Design (*Pure Appl. Chem.*, 1997, **69**, 1137–1152) and in Glossary for Chemists of terms used in Toxicology (*Pure Appl. Chem.* 1993, **65**, 2003–2122), are identified by a double** and a triple*** asterisk respectively.

Active transport*

Active transport is the carriage of a solute across a biological membrane from low to high concentration that requires the expenditure of (metabolic) energy.

Address-message concept

Address-message concept refers to compounds in which part of the molecule is required for binding (address) and part for the biological action (message).

ADME

Abbreviation for **Absorption, Distribution, Metabolism, Excretion**. (See also **Pharmacokinetics; Drug disposition**).

Affinity

Affinity is the tendency of a molecule to associate with another. The **affinity** of a **drug** is its ability to bind to its biological target (**receptor, enzyme,** transport system, etc.) For pharmacological **receptors** it can be thought of as the frequency with which the **drug,** when brought into the proximity of a **receptor** by diffusion, will reside at a position of minimum free energy within the force field of that **receptor.**

For an **agonist** (or for an **antagonist**) the numerical representation of **affinity** is the reciprocal of the equilibrium dissociation constant of the ligand-**receptor** complex denoted K_A, calculated as the rate constant for offset (k_{-1}) divided by the rate constant for onset (k_1).

Agonist***

An **agonist** is an endogenous substance or a **drug** that can interact with a **receptor** and initiate a physiological or a pharmacological response characteristic of that **receptor** (contraction, relaxation, secretion, **enzyme** activation, etc.).

Allosteric binding sites

Allosteric binding sites are contained in many **enzymes** and **receptors**. As a consequence of the binding to **allosteric binding sites**, the interaction with the normal ligand may be either enhanced or reduced.

Allosteric enzyme*

An **allosteric enzyme** is an **enzyme** that contains a region to which small, regulatory molecules ("effectors") may bind in addition to and separate from the substrate binding site and thereby affect the catalytic activity.

On binding the effector, the catalytic activity of the **enzyme** towards the substrate may be enhanced, in which case the effector is an activator, or reduced, in which case it is a de-activator or inhibitor.

Allosteric regulation

Allosteric regulation is the regulation of the activity of **allosteric enzymes**. (See also **Allosteric binding sites; Allosteric enzymes**).

Analog

An **analog** is a **drug** whose structure is related to that of another **drug** but whose chemical and biological properties may be quite different. (See also **Congener**).

Antagonist***

An **antagonist** is a **drug** or a compound that opposes the physiological effects of another. At the **receptor** level, it is a chemical entity that opposes the **receptor**-associated responses normally induced by another bioactive agent.

Antimetabolite***

An **antimetabolite** is a structural **analog** of an intermediate (substrate or **coenzyme**) in a physiologically occurring metabolic pathway that acts by replacing the natural substrate thus blocking or diverting the biosynthesis of physiologically important substances.

Antisense molecule

An **antisense molecule** is an **oligonucleotide** or **analog** thereof that is complementary to a segment of RNA (ribonucleic acid) or DNA (deoxyribonucleic acid) and that binds to it and inhibits its normal function.

Autacoid

An **autacoid** is a biological substance secreted by various cells whose physiological activity is restricted to the vicinity of its release; it is often referred to as local **hormone**.

Autoreceptor

An **autoreceptor**, present at a nerve ending, is a **receptor** that regulates, via positive or negative feedback processes, the synthesis and/or release of its own physiological ligand. (See also **Heteroreceptor**).

Bioassay***

A **bioassay** is a procedure for determining the concentration, purity, and/or biological activity of a substance (e.g., vitamin, **hormone**, plant growth factor, antibiotic, **enzyme**) by measuring its effect on an organism, tissue, cell, **enzyme** or **receptor** preparation compared to a standard preparation.

Bioisostere

A **bioisostere** is a compound resulting from the exchange of an atom or of a group of atoms with another, broadly similar, atom or group of atoms. The objective of a bioisosteric replacement is to create a new compound with similar biological properties to the parent compound. The bioisosteric replacement may be physicochemically or topologically based. (See also **Isostere**)

Bioprecursor prodrug

A **bioprecursor prodrug** is a **prodrug** that does not imply the linkage to a carrier group, but results from a molecular modification of the active principle itself. This modification generates a new compound, able to be transformed metabolically or chemically, the resulting compound being the active principle.

Biotransformation

Biotransformation is the chemical conversion of substances by living organisms or **enzyme** preparations.

CADD

See **Computer-assisted drug design**

Carrier-linked prodrug (Carrier prodrug)

A **carrier-linked prodrug** is a **prodrug** that contains a temporary linkage of a given active substance with a transient carrier group that produces improved physicochemical or pharmacokinetic properties and that can be easily removed *in vivo*, usually by a hydrolytic cleavage.

Cascade prodrug

A **cascade prodrug** is a **prodrug** for which the cleavage of the carrier group becomes effective only after unmasking an activating group.

Catabolism***

Catabolism consists of reactions involving endogenous organic substrates to provide chemically available energy (e.g., ATP) and/or to generate metabolic intermediates used in subsequent anabolic reactions.

Catabolite

A **catabolite** is a naturally occurring **metabolite.**

Clone*

A **clone** is a population of genetically identical cells produced from a common ancestor. Sometimes, "**clone**" is also used for a number of recombinant DNA (deoxyribonucleic acid) molecules all carrying the same inserted sequence.

Codon*

A **codon** is the sequence of three consecutive **nucleotides** that occurs in mRNA which directs the incorporation of a specific amino acid into a protein or represents the starting or termination signals of protein synthesis.

Coenzyme

A **coenzyme** is a dissociable, low-molecular weight, non-proteinaceous organic compound (often **nucleotide**) participating in enzymatic reactions as acceptor or donor of chemical groups or electrons.

Combinatorial synthesis

Combinatorial synthesis is a process to prepare large sets of organic compounds by combining sets of building blocks.

Combinatorial library

A **combinatorial library** is a set of compounds prepared by combinatorial synthesis.

CoMFA

See **Comparative Molecular Field Analysis**

Comparative Molecular Field Analysis (CoMFA)**

Comparative molecular field analysis (CoMFA) is a **3D-QSAR** method that uses statistical correlation techniques for the analysis of the quantitative relationship between the biological activity of a set of compounds with a specified alignment, and their three-dimensional electronic and steric properties. Other properties such as hydrophobicity and hydrogen bonding can also be incorporated into the analysis. (See also **Three-dimensional Quantitative Structure-Activity Relationship [3D-QSAR]**).

Computational chemistry**

Computational chemistry is a discipline using mathematical methods for the calculation of molecular properties or for the simulation of molecular behaviour.

Computer-assisted drug design (CADD)**

Computer-assisted drug design involves all computer-assisted techniques used to discover, design and optimize biologically active compounds with a putative use as **drugs.**

Congener***

A **congener** is a substance literally *con-* (with) *generated* or synthesized by essentially the same synthetic chemical reactions and the same procedures. **Analogs** are substances that are analogous in some respect to the prototype agent in chemical structure.

Clearly **congeners** may be **analogs** or vice versa but not necessarily. The term **congener**, while most often a synonym for homologue, has become somewhat more diffuse in meaning so that the terms **congener** and **analog** are frequently used interchangeably in the literature.

Cooperativity

Cooperativity is the interaction process by which binding of a ligand to one site on a macromolecule (**enzyme, receptor,** etc.) influences binding at a second site, e.g. between the substrate binding sites of an **allosteric enzyme**. Cooperative **enzymes** typically display a sigmoid (S-shaped) plot of the reaction rate against substrate concentration. (See also **Allosteric binding sites**).

3D-QSAR

See **Three-dimensional Quantitative Structure-Activity Relationship**

De novo design**

***De novo* design** is the design of bioactive compounds by incremental construction of a ligand model within a model of the **receptor** or **enzyme** active site, the structure of which is known from X-ray or nuclear magnetic resonance (NMR) data.

Disposition

See **Drug disposition**

Distomer

A **distomer** is the enantiomer of a chiral compound that is the less potent for a particular action. This definition does not excude the possibility of other effect or side effect of the **distomer** (See also **Eutomer**).

Docking studies

Docking studies are molecular modeling studies aiming at finding a proper fit between a ligand and its binding site.

Double-blind study

A ***double-blind study*** is a clinical study of potential and marketed **drugs**, where neither the investigators nor the subjects know which subjects will be treated with the active principle and which ones will receive a placebo.

Double prodrug (or pro-prodrug)

A **double prodrug** is a biologically inactive molecule which is transformed *in vivo* in two steps (enzymatically and/or chemically) to the active species.

Drug***

A **drug** is any substance presented for treating, curing or preventing disease in human beings or in animals. A **drug** may also be used for making a medical diagnosis or for restoring, correcting, or modifying physiological functions (e.g., the contraceptive pill).

Drug disposition

Drug disposition refers to all processes involved in the absorption, distribution **metabolism** and excretion of **drugs** in a living organism.

Drug latentiation

Drug latentiation is the chemical modification of a biologically active compound to form a new compound, which *in vivo* will liberate the parent compound. **Drug latentiation** is synonymous with **prodrug** design.

Drug targeting

Drug targeting is a strategy aiming at the delivery of a compound to a particular tissue of the body.

Dual action drug

A **dual action drug** is a compound which combines two desired different pharmacological actions at a similarly efficacious dose.

Efficacy

Efficacy describes the relative intensity with which **agonists** vary in the response they produce even when they occupy the same number of **receptors** and with the same **affinity**. **Efficacy** *is not* synonymous to **Intrinsic activity**.

Efficacy is the property that enables **drugs** to produce responses. It is convenient to differentiate the properties of **drugs** into two groups, those which cause them to associate with the **receptors** (**affinity**) and those that produce stimulus (**efficacy**). This term is often used to characterize the level of maximal responses induced by **agonists**. In fact, not all **agonists** of a **receptor** are capable of inducing identical levels of maximal responses. Maximal response depends on the efficiency of **receptor** coupling, i.e., from the cascade of events, which, from the binding of the **drug** to the **receptor**, leads to the observed biological effect.

Elimination

Elimination is the process achieving the reduction of of the concentration of a **xenobiotic** including its **metabolism**.

Enzyme*

An **enzyme** is a macromolecule, usually a protein, that functions as a (bio) catalyst by increasing the reaction rate.

In general, an **enzyme** catalyzes only one reaction type (reaction selectivity) and operates on only one type of substrate (substrate selectivity). Substrate molecules are transformed at the same site (regioselectivity) and only one or preferentially one of chiral a substrate or of a racemate is transformed (enantioselectivity[special form of stereoselectivity]).

Enzyme induction*

Enzyme induction is the process whereby an (inducible) **enzyme** is synthesized in response to a specific inducer molecule. The inducer molecule (often a substrate that needs the catalytic activity of the inducible **enzyme** for its **metabolism**) combines with a repressor and thereby prevents the blocking of an operator by the repressor leading to the translation of the gene for the **enzyme**.

Enzyme repression*

Enzyme repression is the mode by which the synthesis of an **enzyme** is prevented by repressor molecules.

In many cases, the end product of a synthesis chain (e.g., an amino acid) acts as a feed-back corepressor by combining with an intracellular aporepressor protein, so that this complex is able to block the function of an operator. As a result, the whole operation is prevented from being transcribed into mRNA, and the expression of all **enzymes** necessary for the synthesis of the end product **enzyme** is abolished.

Eudismic ratio

Eudismic ratio is the **potency** of the **eutomer** relative to that of the **distomer**.

Eutomer

The **Eutomer** is the enantiomer of a chiral compound that is the more potent for a particular action (See also **Distomer**).

Genome*

A **genome** is the complete set of chromosomal and extrachromosomal genes of an organism, a cell, an organelle or a virus; the complete DNA (deoxyribonucleic acid) component of an organism.

Hansch analysis**

Hansch analysis is the investigation of the quantitative relationship between the biological activity of a series of compounds and their physicochemical substituent or global parameters representing hydrophobic, electronic, steric and other effects using multiple regression correlation methodology.

Hapten***

A **hapten** is a low molecular weight molecule that contains an antigenic determinant but which is not itself antigenic unless combined with an antigenic carrier.

Hard drug

A **hard drug** is a nonmetabolizable compound, characterized either by high lipid solubility and accumulation in adipose tissues and organelles, or by high water solubility.

In the lay press the term "**Hard Drug**" refers to a powerful **drug** of abuse such as cocaine or heroin.

Heteroreceptor

A **heteroreceptor** is a **receptor** regulating the synthesis and/or the release of mediators other than its own ligand (See also **Autoreceptor**).

Homologue

The term **homologue** is used to describe a compound belonging to a series of compounds differing from each other by a repeating unit, such as a methylene group, a peptide residue, etc.

Hormone***

A **hormone** is a substance produced by endocrine glands, released in very low concentration into the bloodstream, and which exerts regulatory effects on specific organs or tissues distant from the site of secretion.

Hydrophilicity**

Hydrophilicity is the tendency of a molecule to be solvated by water.

Hydrophobicity**

Hydrophobicity is the association of non-polar groups or molecules in an aqueous environment which arises from the tendency of water to exclude non polar molecules. (See also **Lipophilicity**).

IND

Abbreviation for **Investigational New Drug**.

Intrinsic activity

Intrinsic activity is the maximal stimulatory response induced by a compound in relation to that of a given reference compound (See also **Partial agonist**)

This term has evolved with common usage. It was introduced by Ariëns as a proportionality factor between tissue response and receptor occupancy. The numerical value of intrinsic activity (alpha) could range from unity (for full agonists, i.e., agonist inducing the tissue maximal response) to zero (for antagonists), the fractional values within this range denoting partial agonists. Ariëns' original definition equates the molecular nature of alpha to maximal response only when response is a linear function of receptor occupancy. This function has been verified. Thus, intrinsic activity, which is a drug and tissue parameter, cannot be used as a characteristic drug parameter for classification of drugs or drug receptors. For this purpose, a proportionality factor derived by null methods, namely, relative efficacy, should be used. Finally, "intrinsic activity" should not be used instead of "intrinsic efficacy". A "partial agonist" should be termed "agonist with intermediate intrinsic efficacy" in a given tissue.

Inverse agonist

An **inverse agonist** is a **drug** which acts at the same **receptor** as that of an **agonist**, yet produces an opposite effect. Also called negative **antagonists**.

Isosteres

Isosteres are molecules or ions of similar size containing the same number of atoms and valence electrons, e.g., O^{2-}, F^-, Ne (See also **Bioisostere**).

Latentiated drug

See **Drug Latentiation.**

Lead discovery

Lead discovery is the process of identifying active new chemical entities, which by subsequent modification may be transformed into a clinically useful **drug.**

Lead generation

Lead generation is the term applied to strategies developed to identify compounds which possess a desired but non-optimized biological activity.

Lead optimization

Lead optimization is the synthetic modification of a biologically active compound, to fulfill all stereoelectronic, physicochemical, pharmacokinetic and toxicologic requirements for clinical usefulness.

Lipophilicity**

Lipophilicity represents the **affinity** of a molecule or a moiety for a lipophilic environment. It is commonly measured by its distribution behaviour in a biphasic system, either liquid-liquid (e.g., partition coefficient in octan-1-ol/water) or solid/liquid (retention on reversed-phase high performance liquid chromatography (RP-HPLC) or thin-layer chromatography (TLC) system). (See also **Hydrophobicity).**

Medicinal chemistry

Medicinal chemistry is a chemistry-based discipline, also involving aspects of biological, medical and pharmaceutical sciences. It is concerned with the invention, discovery, design, identification and preparation of biologically active compounds, the study of their **metabolism,** the interpretation of their mode of action at the molecular level and the construction of **structure-activity relationships.**

Metabolism*

The term **metabolism** comprises the entire physical and chemical processes involved in the maintenance and reproduction of life in which nutrients are broken down to generate energy and to give simpler molecules (**catabolism**) which by themselves may be used to form more complex molecules (anabolism).

In case of heterotrophic organisms, the energy evolving from catabolic processes is made available for use by the organism.

In **medicinal chemistry** the term **metabolism** refers to the **biotransformation** of **xenobiotics** and particularly **drugs.** (See also **Biotransformation; Xenobiotic).**

Metabolite

A **metabolite** is any intermediate or product resulting from **metabolism.**

Me-too drug

A **me-too drug** is a compound that is structurally very similar to already known **drugs,** with only minor pharmacological differences.

Molecular graphics**

Molecular graphics is the visualization and manipulation of three-dimensional representations of molecules on a graphical display device.

Molecular modeling**

Molecular modeling is a technique for the investigation of molecular structures and properties using computational chemistry and graphical visualization techniques in order to provide a plausible three-dimensional representation under a given set of circumstances.

Mutagen***

A **mutagen** is an agent that causes a permanent heritable change (i.e., a mutation) into the DNA (deoxyribonucleic acid) of an organism.

Mutual prodrug

A **mutual prodrug** is the association in a unique molecule of two, usually synergistic, **drugs** attached to each other, one **drug** being the carrier for the other and vice versa.

NCE

See **New Chemical Entity**.

NDA

Abbreviation for **New Drug Application**.

New Chemical Entity.

A **new chemical entity (NCE)** is a compound not previously described in the literature.

Non-classical isostere

Same meaning as **Bioisostere**.

Nucleic acid*

A **nucleic acid** is a macromolecule composed of linear sequences of nucleotides that perform several functions in living cells, e.g., the storage of genetic information and its transfer from one generation to the next DNA (deoxyribonucleic acid), the expression of this information in protein synthesis (mRNA, tRNA) and may act as functional components of subcellular units such as ribosomes (rRNA).

RNA (ribonucleic acid) contains D-ribose, DNA contains 2-deoxy-D-ribose as the sugar component.

Nucleoside*

A **nucleoside** is a compound in which a purine or pyrimidine base is bound via a N-atom to C-1 replacing the hydroxy group of either 2-deoxy-D-ribose or of D-ribose, but without any phosphate groups. (See also **nucleotide**).

The common **nucleosides** in biological systems are adenosine, guanosine, cytidine, and uridine (which contain ribose) and deoxyadenosine, deoxyguanosine, deoxycytidine and thymidine (which contain deoxyribose).

Nucleotide

A **nucleotide** is a **nucleoside** in which the primary hydroxy group of either 2-deoxy-D-ribose or of D-ribose is esterified by orthophosphoric acid. (See also **nucleoside**).

Oligonucleotide

An **oligonucleotide** is an oligomer resulting from a linear sequences of nucleotides.

Oncogene***

An **oncogene** is a normal cellular gene which, when inappropriately expressed or mutated, can transform eukaryotic cells into tumour cells.

Orphan drug

An **orphan drug** is a **drug** for the treatment of a rare disease for which reasonable recovery of the sponsoring firm's research and development expenditure is not expected within a reasonable time. The term is also used to describe substances intended for such uses.

Partial agonist

A **partial agonist** is an **agonist** which is unable to induce maximal activation of a **receptor** population, regardless of the amount of **drug** applied (See also **Intrinsic activity**).

Pattern recognition**

Pattern recognition is the identification of patterns in large data sets using appropriate mathematical methodologies.

Peptidomimetic

A **peptidomimetic** is a compound containing non-peptidic structural elements that is capable of mimicking or antagonizing the biological action(s) of a natural parent peptide. A peptidomimetic does no longer have classical peptide characteristics such as enzymatically scissille peptidic bonds. (See also **peptoids**).

Peptoid

A **peptoid** is a **peptidomimetic** that results from the oligomeric assembly of N-substituted glycines.

Pfeiffer's rule

Pfeiffer's rule states that in a series of chiral compounds the **eudismic ratio** increases with increasing **potency** of the **eutomer**.

Pharmacokinetics***

Pharmacokinetics refers to the study of absorption, distribution, **metabolism** and excretion (**ADME**) of bioactive compounds in a higher organism. (See also**Drug disposition**).

Pharmacophore (pharmacophoric pattern)

A **pharmacophore** is the ensemble of steric and electronic features that is necessary to ensure the optimal supramolecular interactions with a specific biological target structure and to trigger (or to block) its biological response.

A **pharmacophore** does not represent a real molecule or a real association of functional groups, but a purely abstract concept that accounts for the common molecular interaction capacities of a group of compounds towards their target structure. The **pharmacophore** can be considered as the largest common denominator shared by a set of active molecules. This definition

discards a misuse often found in the **medicinal chemistry** literature which consists of naming as **pharmacophores** simple chemical functionalities such as guanidines, sulfonamides or dihydroimidazoles (formerly imidazolines), or typical structural skeletons such as flavones, phenothiazines, prostaglandins or steroids.

Pharmacophoric descriptors

Pharmacophoric descriptors are used to define a **pharmacophore**, including H-bonding, hydrophobic and electrostatic interaction sites, defined by atoms, ring centers and virtual points.

Placebo

A **placebo** is an inert substance or dosage form which is identical in appearance, flavor and odour to the active substance or dosage form. It is used as a negative control in a **bioassay** or in a clinical study.

Potency***

Potency is the dose of **drug** required to produce a specific effect of given intensity as compared to a standard reference.

Potency is a comparative rather than an absolute expression of **drug** activity. **Drug potency** depends on both **affinity** and **efficacy**. Thus, two **agonists** can be equipotent, but have different intrinsic efficacies with compensating differences in **affinity**.

Prodrug

A **prodrug** is any compound that undergoes **biotransformation** before exhibiting its pharmacological effects. **Prodrugs** can thus be viewed as **drugs** containing specialized non-toxic protective groups used in a transient manner to alter or to eliminate undesirable properties in the parent molecule . (See also **Double prodrug**).

QSAR

See **Quantitative Structure-Activity Relationships**

Quantitative Structure-Activity Relationships (QSAR)**

Quantitative structure-activity relationships are mathematical relationships linking chemical structure and pharmacological activity in a quantitative manner for a series of compounds. Methods which can be used in **QSAR** include various regression and **pattern recognition** techniques.

Receptor*

A **receptor** is a molecule or a polymeric structure in or on a cell that specifically recognizes and binds a compound acting as a molecular messenger (neurotransmitter, **hormone**, lymphokine, lectin, **drug**, etc.).

Receptor mapping**

Receptor mapping is the technique used to describe the geometric and/or electronic features of a binding site when insufficient structural data for this **receptor** or **enzyme** are available. Generally the active site cavity is defined by comparing the superposition of active to that of inactive molecules.

Second messenger

A **second messenger** is an intracellular **metabolite** or ion increasing or decreasing as a response to the stimulation of **receptors** by **agonists**, considered as the "first messenger". This generic term usually does not prejudge the rank order of intracellular biochemical events.

Site-specific delivery

Site-specific delivery is an approach to target a **drug** to a specific tissue, using **prodrugs** or antibody recognition systems.

Soft drug

A **soft drug** is a compound that is degraded *in vivo* to predictable non-toxic and inactive **metabolites**, after having achieved its therapeutic role.

SPC

See **Structure-property correlations**

Structure-activity relationship (SAR)

Structure-activity relationship is the relationship between chemical structure and pharmacological activity for a series of compounds.

Structure-based design**

Structure-based design is a **drug** design strategy based on the 3D structure of the target obtained by X-ray or NMR.

Structure-property correlations (SPC)**

Structure-property correlations refers to all statistical mathematical methods used to correlate any structural property to any other property (intrinsic, chemical or biological), using statistical regression and **pattern recognition** techniques.

Systemic***

Systemic means relating to or affecting the whole body.

Teratogen***

A **teratogen** is a substance that produces a malformation in a foetus.

Three-dimensional Quantitative Structure-Activity Relationship (3D-QSAR)

A **three-dimensional quantitative structure-activity relationship** is the analysis of the quantitative relationship between the biological activity of a set of compounds and their spatial properties using statistical methods.

Topliss tree**

A **Topliss tree** is an operational scheme for **analog** design.

Transition-state analog

A **transition-state analog** is a compound that mimics the transition state of a substrate bound to an **enzyme**.

Xenobiotic***

A **xenobiotic** is a compound foreign to an organism (xenos [greek] = foreign).

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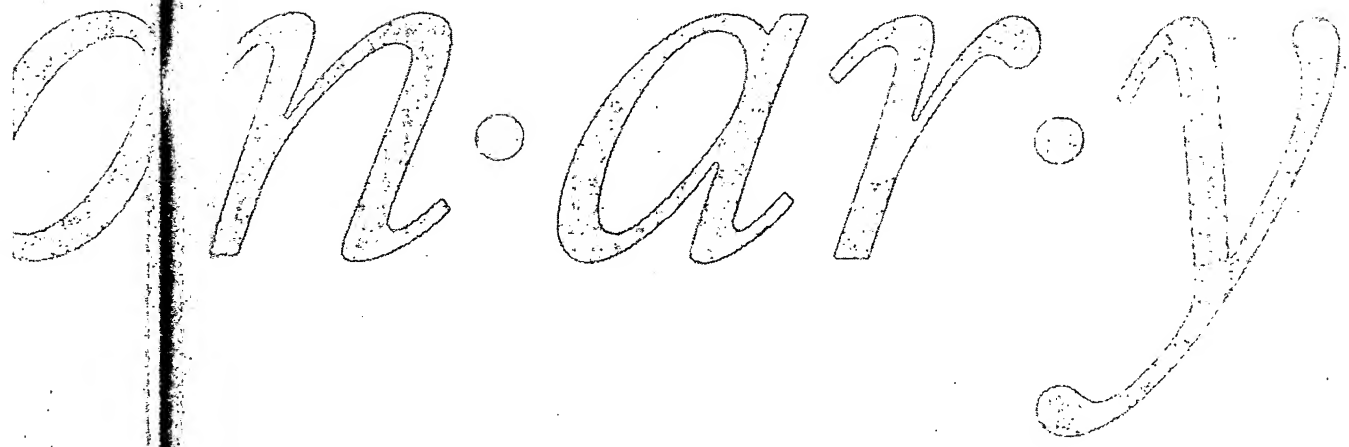

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anal-retentive. [< Lat. *ānus*, anus.] — **a′nal•ly** *adv.*

anal. *abbr.* 1. Analogous; analogy. 2. Analysis; analytic.

a•nal•cime (ə-năl′sēm′) also **a•nal•cite** (-sīt′) *n.* A zeolite, $NaAlSi_2O_6 \cdot H_2O$, found in certain basalts. [Fr. < Gk. *analkimos*, weak (from its weak electric power) : *an-*, not; see A-[1] + *alkimos*, brave (< *alkē*, strength).] — **a•nal•cim′ic** *adj.*

an•a•lects (ăn′ə-lĕkts′) also **an•a•lec•ta** (ăn′ə-lĕk′tə) *pl.n.* Selections from or parts of a literary work or group of works. [Gk. *analekta*, selected things < neut. pl. of *analektos*, gathered together < *analegein*, to gather : *ana-*, ana- + *legein*, to gather; see **leg-***.] — **an′a•lec′tic** *adj.*

an•a•lem•ma (ăn′ə-lĕm′ə) *n.* A graduated scale in the shape of a figure eight, indicating the sun's declination and the equation of time for every day of the year. [Lat., sundial < Gk. *analēmma* < *analambanein*, to take up. See ANALEPTIC.]

an•a•lep•tic (ăn′ə-lĕp′tĭk) *adj.* Restorative or stimulating, as a drug or medication. — *n.* A medication used as a central nervous system stimulant. [Gk. *analēptikos* < *analambanein*, to take up : *ana-*, ana- + *lambanein*, *lēp-*, to take.]

a•nal-ex•pul•sive (ā′nəl-ĭk-spŭl′sĭv) *adj. Psychol.* In psychoanalytic theory, of or relating to personality traits, such as conceit, suspicion, ambition, and generosity, originating in infantile pleasure in expelling feces.

an•al•ge•si•a (ăn′əl-jē′zē-ə, -zhə) *n. Pathol.* A deadening or absence of pain without loss of consciousness. [Gk. *analgēsia*: *an-*, without; see A-[1] + *algēsia*, pain (< *algein*, to feel pain < *algos*, pain).] — **an′al•get′ic** (-jĕt′ĭk) *adj.*

an•al•ge•sic (ăn′əl-jē′zĭk, -sĭk) *n.* A medication that reduces or eliminates pain. — *adj.* Of or causing analgesia.

an•a•log (ăn′ə-lôg′, -lŏg′) *n. & adj.* Var. of **analogue.**

analog computer also **analogue computer** *n. Comp. Sci.* A computer in which numerical data are represented by measurable physical variables, such as electrical signals.

an•a•log•i•cal (ăn′ə-lŏj′ĭ-kəl) *adj.* Of, expressing, composed of, or based on an analogy. — **an′a•log′i•cal•ly** *adv.*

a•nal•o•gist (ə-năl′ə-jĭst) *n.* One who seeks or reasons by analogy.

a•nal•o•gize (ə-năl′ə-jīz′) *v.* **-gized, -giz•ing, -giz•es.** — *tr.* To make an analogy to. — *intr.* To seek or reason by analogy.

a•nal•o•gous (ə-năl′ə-gəs) *adj.* 1. Similar in such a way as to permit analogy. 2. *Biol.* Similar in function but not in structure and evolutionary origin. [< Lat. *analogus* < Gk. *analogos*, proportionate : *ana-*, according to; see ANA- + *logos*, proportion; see **leg-***.] — **a•nal′o•gous•ly** *adv.* — **a•nal′o•gous•ness** *n.*

an•a•logue also **an•a•log** (ăn′ə-lôg′, -lŏg′) — *n.* 1. Something that bears an analogy to something else. 2. *Biol.* An organ or structure similar in function to one in another kind of organism but of dissimilar evolutionary origin. 3. *Chem.* A structural derivative of a parent compound that often differs from it by a single element. — *adj.* 1. Often **analog.** Of, relating to, or being a device in which data are represented by variable measurable physical quantities. 2. Often **analog.** *Comp. Sci.* Of or relating to an analog computer. [Fr., analogous, analogue < Med.Lat. *analogus* < Gk. *analogos*, proportionate. See ANALOGOUS.]

a•nal•o•gy (ə-năl′ə-jē) *n., pl.* **-gies.** 1.a. Similarity in some respects between things that are otherwise dissimilar. b. A comparison based on such similarity. See Syns at **likeness.** 2. *Biol.* Correspondence in function or position between organs of dissimilar evolutionary origin or structure. 3. A form or instance of logical inference, based on the assumption that if two things are alike in some respects, they must be alike in other respects. 4. *Ling.* The process by which words and morphemes are re-formed or created on the model of existing grammatical patterns, as *name : names* for Old English *nama : naman* on the model of nouns like *stone : stones*. [ME *analogie* < OFr. < Lat. *analogia* < Gk. < *analogos*, proportionate. See ANALOGOUS.]

an•al•pha•bet•ic (ăn-ăl′fə-bĕt′ĭk) *adj.* 1. Not alphabetical. 2. Unable to read; illiterate. — *n.* One who is unable to read; an illiterate. [< Gk. *analphabētos*, not knowing the alphabet : *an-*, not; see A-[1] + *alphabētos*, alphabet; see ALPHABET.]

a•nal•re•ten•tive (ā′nəl-rī-tĕn′tĭv) *adj.* In psychoanalytic theory, of or relating to personality traits, such as meticulousness, avarice, and obstinacy, originating in infantile pleasure in retention of feces.

a•nal•y•sand (ə-năl′ī-sănd′) *n.* A person who is being psychoanalyzed. [< ANALYZE, on the model of MULTIPLICAND.]

a•nal•y•sis (ə-năl′ī-sĭs) *n., pl.* **-ses** (-sēz′). 1. The separation of a whole into its constituent parts for individual study. 2. *Chem.* a. The separation of a substance into its constituent elements to determine either their nature (qualitative analysis) or their proportions (quantitative analysis). b. The stated findings of such a procedure. 3. *Math.* a. A branch of mathematics principally involving calculus, sequences, and series and concerned with limits and convergence. b. The method of proof in which a known truth is sought as a consequence of deductions from that which is to be proved. 4. *Ling.* The use of function words such as prepositions instead of inflectional endings to express a grammatical relationship; for example, *the paw of the dog* instead of *the dog's paw.* 5. Psychoanalysis. 6. Systems analysis. [Med.Lat. < Gk. *analusis*, a ... ing < *analuein*, to undo : *ana-*, throughout; see ANA- + ... to loosen; see **leu-***.]

an•a•lyst (ăn′ə-lĭst) *n.* 1. One that analyzes. 2. A ... practitioner of psychoanalysis. 3. A systems analyst.

an•a•lyt•ic (ăn′ə-lĭt′ĭk) or **an•a•lyt•i•cal** (-ĭ-kəl) *adj.* ... or relating to analysis or analytics. 2. Dividing into ... parts or basic principles. 3. Reasoning from a percep... the parts and interrelations of a subject. 4. Expert in or ... analysis, esp. in thinking: *an analytic mind.* 5. *Logic.* ... ing necessarily; tautologous. 6. *Math.* a. Using or capa... being subjected to a methodology involving algebra an... culus. b. Proving a known truth by reasoning from that ... is to be proved. 7. *Ling.* Expressing a grammatical ca... with two or more words instead of an inflected form. 8. ... choanalytic. [Med.Lat. *analȳticus* < Gk: *analutikos* ... *luein*, to resolve. See ANALYSIS.] — **an′a•lyt′i•cal•ly** *adv.*

analytical balance *n.* A balance for chemical analysis.

analytic geometry *n. Math.* The analysis of geometric ... tures and properties principally by algebraic operation... variables defined in terms of position coordinates.

an•a•lyt•ics (ăn′ə-lĭt′ĭks) *n. (used with a sing. or pl. v.)* ... branch of logic dealing with analysis.

an•a•lyze (ăn′ə-līz′) *tr.v.* **-lyzed, -lyz•ing, -lyz•es.** 1. To ... arate into parts or basic principles so as to determine ... nature of the whole; examine methodically. 2. *Chem.* ... make a chemical analysis of. 3. *Math.* To make a mathe... ical analysis of. 4. To psychoanalyze. [Perh. < Fr. *analyse*, analysis < Gk. *analusis*. See ANALYSIS.] — **an′a•ly•za′ble** *adj.* — **an′a•ly•za′tion** *n.* — **an′a•lyz′er** *n.*

Syns: analyze, anatomize, dissect, resolve. The ... meaning shared by these verbs is "to separate into constit... parts for study": *analyzed a chemical substance; anatomi... the doctrine of free enterprise; medical students dissecting ... cadavers; vapor resolved into water.*

an•am•ne•sis (ăn′ăm-nē′sĭs) *n., pl.* **-ses** (-sēz): 1. *Psych...* recalling to memory; recollection. 2. *Medic.* The com... case history of a patient. [Gk. *anamnēsis* < *anamimnēsk...* to remind : *ana-*, ana- + *mimnēskein*, to recall; see men...] — **an′am•nes′tic** (-nĕs′tĭk) *adj.* — **an′am•nes′ti•cal•ly** *adv.*

an•a•mor•phic (ăn′ə-môr′fĭk) *adj.* Having, producing, or ... ing different optical magnifications along mutually perpen... ular radii. [< ANAMORPHOSIS.]

an•a•mor•pho•sis (ăn′ə-môr′fə-sĭs) *n., pl.* **-ses** (-sēz) ... 1.a. An image that appears distorted unless viewed from ... special angle or with a special instrument. b. The producti... of such an image. 2. Evolutionary increase in complexity ... form and function. [NLat. < LGk. *anamorphoun*, to tra... form : Gk. *ana-*, ana- + Gk. *morphē*, shape.]

An•a•ni•as (ăn′ə-nī′əs). In the Bible, a liar who died wh... Peter rebuked him.

An•an•ke (ə-năng′kē, ə-năn′-) *n.* A satellite of Jupiter. [... *Anankē*, mother of Adrasteia, distributor of rewards and p... ishments, by Jupiter < *anankē*, necessity.]

an•a•pest also **an•a•paest** (ăn′ə-pĕst′) *n.* 1. A metrical ... of two short syllables followed by one long one, as in *at ... park.* 2. A line of verse using this meter. [Lat. *anapestus* ... Gk. *anapaistos*: *ana-*, ana- + *paiein*, *pais-*, to strike (so ca... because an anapest is a reversed dactyl); see **peu-***.] — **a•pes′tic** *adj.*

an•a•phase (ăn′ə-fāz′) *n. Biol.* The stage of mitosis and m... osis in which the chromosomes move to opposite ends of ... nuclear spindle.

a•naph•o•ra (ə-năf′ər-ə) *n.* The repetition of a word or phr... at the beginning of several successive verses, clauses, or p... agraphs. [LLat. < Gk. < *anapherein*, to bring back : *ana-* ... *pherein*, to carry; see **bher-1***.]

an•aph•ro•dis•i•a (ăn-ăf′rə-dĭz′ē-ə, -dĭzh′ə) *n.* Decline ... absence of sexual desire. [Gk., want of power to inspire lo... : *an-*, without; see A-[1] + *aphrodisia*, sexual pleasures; ... APHRODISIAC.] — **an•aph′ro•dis′i•ac′** (ăn-ăf′rə-dĭz′ē-ăk′) ... *adj. & n.*

anaphylactic shock *n.* A sudden, severe and sometimes fat... allergic reaction marked by a sharp drop in blood pressur... urticaria, and breathing difficulties caused by exposure to ... foreign substance after a preliminary exposure.

an•a•phy•lax•is (ăn′ə-fə-lăk′sĭs) *n.* 1. Hypersensitivity ex... in animals to a substance, induced by a small preliminar... exposure to the substance. 2. See **anaphylactic shock.** [ANA- ... + (PRO)PHYLAXIS.] — **an′a•phy•lac′tic** (-lăk′tĭk), **an′a•phy•lac′toid** (-toid) *adj.* — **an′a•phy•lac′ti•cal•ly** *adv.*

an•a•pla•sia (ăn′ə-plā′zhə) *n.* Reversion of cells to an imma... ture or a less differentiated form, as in most malignant t... mors.

an•a•plas•tic (ăn′ə-plăs′tĭk) *adj.* 1. *Medic.* Relating to th... surgical restoration of a lost or absent part. 2. Of o... characterized by cells that have become less differentiated.

A•ná•po•lis (ä-nä′pōō-lĭs). A city of central Brazil SE of Bra... sília. Pop. 160,571.

an•arch (ăn′ärk′) *n.* An adherent of anarchy or a leader prac... ticing it. [Back-formation < ANARCHY.]

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BASIC TERMINOLOGY OF STEREOCHEMISTRY

(IUPAC Recommendations 1996)

Prepared for publication by

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Continued on following page.

447 (1966), *Angew. Chem. Internat. Ed. Eng.* **5**, 385-415, 511 (1966). See also axial chirality: Δ *(delta)*, Λ *(lambda)*.

Heterotopic See *stereoheterotopic*.

Hindered Rotation See *free rotation, hindered rotation, restricted rotation.*

Homochiral See *enantiomerically pure/enantiopure.*

Homomorphic

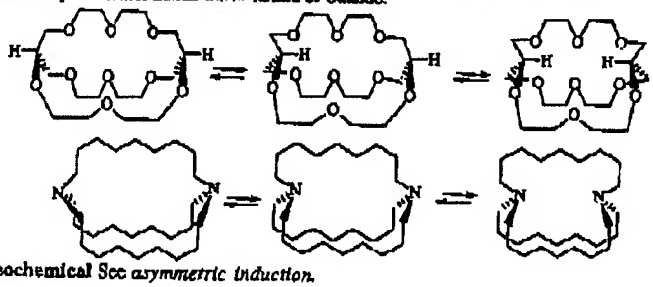
Superposable ligands are called homomorphic.

Homotopic

Atoms or groups of a molecule which are related by an *n*-fold rotation axis ($n = 2, 3,$ *etc*) are called homotopic. For example, chiral tartaric acid (C_2 axis), chloroform (C_3 axis) and cyclohexaamylose (α-cyclodextrin, C_6 axis) have respectively two homotopic carboxyl groups, three homotopic chlorine atoms and six homotopic D-glucose residues. See *prochirality*.

In-Out Isomerism

Isomerism found in bicyclic systems having long enough bridges to allow the bridgehead exocyclic bond or lone pair of electrons to point either inside the structure or outside.



Induction, Stereochemical See *asymmetric induction.*

Internal Compensation (usage strongly discouraged) See *meso*-compound.

Inversion

1. See *Walden inversion.*

2. See *pyramidal inversion.*

3. See *ring inversion.*

4. A symmetry operation involving a centre of inversion (*i*).

Isomer

One of several chemical species (or molecular entities) that have the same stoichiometric molecular formula but different constitutional formulae or different *stereochemical formulae* and hence potentially different physical and/or chemical properties.

Isomeric

Adjective derived from *isomer*.

Isomerism

The relationship between *isomers*.

Isometric, Anisometric

Two molecular entities that are superposable or can be made superposable by reflection of one of them in a mirror are isometric; otherwise they are anisometric.